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May 17, 1999

Dockets Management Branch
Food and Drug Administration (HFA-305)
5630 Fishers Lane
Room 1061
Rockville, MD 20852

By Hand Delivery

Re: Docket No. 98D-0481
Guidance on 180-Day Generic Drug Exclusivity
Further Comments of Teva Pharmaceuticals USA, Inc.

Dear Sir/Madam:

On behalf of Teva Pharmaceuticals USA, Inc. ("Teva"), we respectfully submit these additional comments to the above-referenced guidance (the "180-Day Guidance") in order to respond to a submission to this docket by Andrx Corporation ("Andrx") on January 26, 1999 (Docket Entry C13) ("Andrx Comment").

In its comment, Andrx attempts to justify its claim to a future 180-day period of "exclusivity" for its generic version of Cardizem® CD (diltiazem HCl capsules, extended release) ("diltiazem ER"), and to defend its deal with Hoechst Marion Roussel, Inc. ("HMR"), the patent holder for Cardizem CD, under which Andrx will indefinitely withhold its generic diltiazem ER from the market in exchange for payments of $10 million per quarter from HMR. Because Andrx is the first company to have submitted an application for generic diltiazem ER with a paragraph (iv) certification, other applicants' paragraph (iv) generic diltiazem ER applications may not obtain final effective approval until 180 days after the earlier of (1) Andrx's first commercial marketing of its diltiazem ER product (the "commercial marketing trigger"), or (2) a qualifying court decision under the "court decision trigger." 21 U.S.C. § 355(j)(5)(B)(iv), 21 C.F.R. § 314.107(c). Hence, as Andrx interprets the law, so long as Andrx withholds its diltiazem ER product from the market, this statutory 180-day delay period will not begin (unless there is a court decision that starts the court decision trigger), and no other company's generic diltiazem ER product will be able to enter the market.

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Obviously, however, Andrx's deal with HMR removes any incentive for Andrx to market its own generic diltiazem ER product – which received final FDA approval in July 1998 – thus potentially locking up the generic diltiazem market until the relevant HMR patents expire many years in the future. And now, through its recently announced settlement agreement with Faulding/Purepac, the second paragraph (iv) applicant for generic diltiazem ER, HMR has ensured that its patent litigation against Faulding/Purepac will not lead to a court decision, thus closing off that potential route to activation of the court decision trigger and making sure that HMR's deal with Andrx will continue to block the generic market for the foreseeable future.[1] The only other pending application for generic diltiazem ER is that of Biovail International Corporation ("Biovail"), which, as discussed below, is subject to legal restrictions pursuant to an earlier patent litigation settlement with HMR that may limit its ability to bring a declaratory judgment action against HMR that could activate the court decision trigger. HMR has therefore now removed any possibility that any of the three applicants for generic diltiazem ER will trigger the 180-day delay period applicable to Andrx's application, and has thus succeeded in exploiting the statutory 180-day delay provision to gain effective control of access to the generic diltiazem ER market. This state of affairs is utterly repugnant to Congress's intent in establishing the Hatch-Waxman approval scheme for generic drugs, and should not be tolerated by FDA.

Several prior comments to this Docket, including comments submitted by the Generic Pharmaceutical Industry Association ("GPIA") (C11), Senator Barbara Mikulski (D-Md.) (C5), Agvar Chemicals Inc. (C7), Alfred B. Engelberg, Esq. (C2, C3), Biovail (C9), and Teva (C12), addressed the tremendous harm that can result from deals between patent holders and first generic applicants whereby the first generic applicant agrees to withhold its product from the market in exchange for payment from the patent holder, effectively placing the entire generic market for that product under the collusive control of the first generic applicant and the patent holder. Andrx's recent submission is evidently an attempt to respond to these previous comments.

Andrx spends a great deal of time explaining why a generic applicant should not be required to market its product while that applicant is still involved in litigation with the patent holder, as if this explanation somehow refuted previous comments objecting to collusive deals between first generic applicants and patent holders. In reality, however,

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[1] A copy of the press release announcing the HMR-Faulding/Purepac settlement is attached.

no one has asserted that a generic applicant should be required to market its product while its patent litigation is still pending. Quite the contrary, if all Andrx were doing was to voluntarily refrain from marketing its product until the completion of its current patent litigation with HMR, Teva would emphatically support its right to do so under current law and regulations, as would, presumably, most of the other commenters on this matter.

In fact, however, Andrx has done much more. It has contractually bound itself not to market its drug, in exchange for substantial payments from the patent holder, for an indefinite period of time. It has also protected itself by obtaining a promise from HMR that, if Andrx prevails in the patent litigation, it will be "made whole" through an upward adjustment of the annual $40 million payment from HMR in order to reflect the profits it would have obtained had it been on the market. If Andrx does not prevail in the litigation, however, it will have the right to license Cardizem CD from HMR without having to return any of the payments it received from HMR during the litigation. Through this no-lose arrangement, Andrx has removed any motivation it might have had to market its own product, thoroughly subverting the basic statutory goal of providing incentives to bring generic drugs to market as soon as possible.

Equally objectionable is the fact that the Andrx-HMR deal has removed any incentive for either party to pursue the patent litigation to a conclusion. So long as that litigation continues, HMR receives the tremendous benefit of blocking all generic competition to Cardizem CD by virtue of having locked up the first generic applicant – thus preventing the commercial marketing trigger (as Andrx and HMR see it) from being activated – and Andrx receives the substantial windfall of $10 million a quarter for doing nothing. Notwithstanding Andrx's listing of various motions it has filed (Andrx Comment at 4 n.1), presumably in order to demonstrate the diligence with which it is pursuing this litigation, the fact remains that after more than three years, the litigation is still underway with no end in sight. As the court in Mova Pharmaceutical Corp. v. Shalala stated with regard to the Andrx-HMR diltiazem ER deal: "Under these circumstances, neither party would seem to have maximum incentive to bring the [patent] litigation to a close." 140 F.3d 1060, 1072 n. 14.

Andrx's attempt to justify the business logic of this deal in more legitimate-sounding terms does not work. The payments from HMR, according to Andrx, are "compensation for maintaining the status quo," Andrx Comment at 5. But why should HMR have to pay Andrx "compensation for maintaining the status quo" when, by its own admission on the same page, Andrx would be unwilling in any event to take the risk of marketing its diltiazem ER product while the litigation is ongoing? And would HMR

really have agreed to pay Andrx $40 million a year to keep Andrx's product off the market if other generic companies could enter the market without regard to Andrx? Indeed, the very idea of a generic applicant receiving payment from a brand name company to "maintain the status quo" by withholding a generic product from the market, when there would otherwise be no legal bar to selling that generic product, is antithetical to the fundamental intent of Hatch-Waxman in general and the 180-day delay provision in particular – which is to expedite the market entry of generic drugs.

It could not be more obvious that this deal is not a good faith bargain to preserve the parties' status pending litigation, but a collusive arrangement to take advantage of Andrx's position as first filer in order to extend HMR's patent monopoly and close off the market for generic diltiazem ER. The arrangement plainly benefits HMR by allowing it to prolong its de facto monopoly over the diltiazem ER market, and benefits Andrx by allowing it to receive $40 million annually – and additional amounts if Andrx wins the case – while still allowing Andrx to claim the benefit of the 180-day "exclusivity" following resolution of the litigation. As Teva and other commenters have pointed out, such an arrangement grossly violates the intent and spirit of the Hatch-Waxman Amendments by exploiting the 180-day delay provision for the purpose of blocking the generic market, rather than opening that market.

Andrx also admits that if it does not win the patent case (i.e., loses or settles), it will receive a license from HMR to market Cardizem CD, presumably as a so-called "generic" diltiazem ER. Such an outcome will, of course, only serve to prolong the shared monopolistic control that HMR and Andrx are now enjoying over the diltiazem ER market. Andrx and HMR will no doubt argue that Andrx's marketing of a licensed "generic" Cardizem CD will still not activate the commercial marketing trigger, because it will not constitute commercial marketing under the Andrx ANDA, as the statute contemplates. But Andrx will not be able to market diltiazem ER under its own ANDA until patent expiration, because it will presumably have amended its ANDA to a paragraph (iii) application in response to either losing the patent case or settling the case out. Therefore the market will, under this interpretation, be blocked to true generic versions of Cardizem CD until the HMR patents expire. Having thus prevented true generic competition, HMR and Andrx will be free to maintain higher prices for diltiazem ER, subverting the intent of Hatch-Waxman and causing further economic damage to the public, while enriching themselves. In this light, Andrx's protestation that such a licensing arrangement would be "beneficial to consumers," Andrx Comment at 5, is simply grotesque. Consumers benefit from lower prices brought about by open generic

competition, not from deals that enrich individual drug companies while depriving the public of access to lower-cost generic drugs.

This scenario is more than speculation. It has already occurred as a consequence of the deal struck between Barr Laboratories, Inc. ("Barr") and Zeneca Limited ("Zeneca") over the breast cancer drug tamoxifen citrate after Zeneca was defeated in its patent suit against Barr at the district court level. Under that deal, Zeneca paid Barr $21 million and licensed Barr to sell Zeneca's tamoxifen as a "generic" version of the drug. In exchange, Barr agreed to drop its challenge to Zeneca's tamoxifen patent. Thus, Barr has since 1994 marketed a "generic" tamoxifen for a few dollars less than the branded drug, while vociferously maintaining its claim to a 180-day "exclusivity" that cannot start, according to Barr, until Barr markets tamoxifen under its own ANDA – which cannot now occur until the patent expires, because Barr amended its ANDA to a paragraph (iii) application pursuant to its settlement with Zeneca.[2] Unless FDA takes action to correct the situation, diltiazem ER – and other drugs – may very well end up in the same stranglehold.

It is important to note that through its collusive bargain with Andrx, HMR has not only improperly manipulated the Hatch-Waxman statutory provisions to its own advantage, but has also circumvented the terms of the 1996 consent order with the Federal Trade Commission ("FTC") under which HMR's parent, Hoechst AG, was permitted to acquire Marion Merrell Dow Inc. ("MMD") in the merger that resulted in HMR's formation. A primary basis for the FTC's objection to the merger was the loss of potential competition in the diltiazem ER market. For that reason, the FTC imposed various requirements upon the merger intended to ensure the maintenance of competition in that market.

Through its deal with Andrx, however, HMR has now succeeded in removing Andrx's incentive to market a generic diltiazem ER in competition with Cardizem CD, thus defeating the clear purpose of the FTC consent order. In addition, the terms of a prior settlement of patent litigation between HMR's predecessor and Biovail in connection with the Hoechst/MMD merger may possibly restrict Biovail's ability to

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[2] At present there are two other companies – Pharmachemie B.V. (a subsidiary of Teva) and Mylan Pharmaceuticals Inc. – that hold tentative approvals for generic tamoxifen, but are being blocked from the market by the Barr-Zeneca deal. The tamoxifen situation is described in detail in the various submissions to Docket No. 98P-0493, and is now the subject of a pending lawsuit in U.S. District Court for the District of Columbia (Pharmachemie, B.V. v. Henney, No. 99CV801).

pursue a declaratory judgment action against HMR, potentially blocking another pathway to activation of the court decision trigger in this situation.[3] Thus, HMR has managed to turn the legal arrangements made in connection with the Hoechst/MMD merger – arrangements designed to ensure that the merger would not stifle competition in the diltiazem ER market – into a tool to forestall any generic competition to Cardizem CD by blocking the operation of both the commercial marketing trigger and the court decision trigger for generic diltiazem ER products.

Most recently, HMR has put the final nail in the coffin of a free diltiazem ER market by entering into a settlement of its patent litigation with Faulding/Purepac. This settlement provides that both sides will drop all pending claims in the patent litigation and that Faulding/Purepac's diltiazem ER product will remain off the market until Andrx's 180-day delay period has run. HMR has thereby ensured that Faulding /Purepac, whose diltiazem ER product was tentatively approved in October 1998, will not bring its product to market once its 30-month stay on final approval expires this coming July. HMR has also ensured that there will not be a court decision in its patent case with Faulding/Purepac that will start the 180-day delay clock applicable to Andrx's diltiazem ER. This means that the last remaining potential escape route from the market stranglehold imposed by the HMR-Andrx deal has now been closed off. Clearer evidence of HMR's blatant manipulation of the 180-day delay provision to extend its monopoly on diltiazem ER would be impossible to imagine.

Those who have submitted comments to this docket have put forth various solutions to prevent this type of abuse. Teva and others have suggested that the sale by a first generic applicant of its right to market its drug should be viewed as "commercial marketing" within the meaning of the statute. This solution would recognize that by entering into the kind of deal Andrx and HMR have struck, the first generic applicant has commercially marketed its product in the only sense that counts: it has bargained away its property right in the product in exchange for valuable commercial consideration. This solution would also uphold the clear intent of Hatch-Waxman by expediting, rather than hindering, the entry of lower-cost generic drugs onto the market.

In response to these proposals, Andrx asserts that the "marketing exclusivity" provision of the statute was "intended to give a valuable right to the first-filed ANDA

[3] The declaratory judgment mechanism for activating the court decision trigger is discussed in detail in GPIA's comment to this docket (C11).

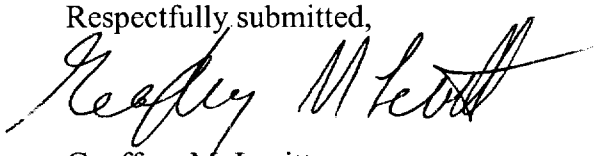
applicant," and that the "mere exercise of that right should not deprive the company exercising it of the right itself," Andrx Comment at 3. This is false. Nowhere does the applicable provision of the statute speak of a "right" or even, for that matter, of "exclusivity." All that it does is to establish a defined period of delay in the effective approval of subsequent ANDAs based on a complex statutory scheme that carefully balances the need to encourage generic applicants to challenge patents, on the one hand, with the overriding goal of getting generic drugs onto the market quickly, on the other hand. Andrx's view of the world would entirely discard the latter (and more important) part of this statutory balance and award the first filer some kind of absolute "right" to "exclusivity" that must be upheld at all costs – even when, as here, that right threatens to deprive consumers of generic drugs altogether. Contrary to Andrx's interpretation, the incentive Congress provided through the 180-day delay period was not meant to overshadow the rest of the statute in this way.[4]

In a feeble attempt to demonstrate that there is no need for new solutions to the problem of generic market blockage through deals such as the one it has struck with HMR, Andrx asserts that FDA regulations, specifically 21 C.F.R. § 314.107(c)(4), require a generic applicant that is not sued by the patent holder to "launch its product as soon as possible." Andrx Comment at 1. This is false. The FDA regulation in question merely defines when "commercial marketing" will be considered to commence for purposes of beginning the 180-day delay clock under 21 U.S.C. § 505(j)(5)(B)(iv)(I). It says nothing whatsoever about any "requirement" that the applicant begin such marketing at any specific time, or ever.

[4] Significantly, the 180-Day Exclusivity Guidance itself refutes Andrx's position that the first applicant has an absolute right to exclusivity by acknowledging that the court decision trigger can be activated by a decision in a patent case involving a subsequent applicant, Guidance at 5. Inasmuch as such a situation could result, under various circumstances, in the 180-day delay period elapsing without the first filer having marketed its drug at all, it necessarily follows that any "right" to "exclusivity" is subordinate to the workings of the court decision and commercial marketing triggers.

In sum, Andrx's attempt to justify its deal with HMR as pro-competitive, pro-consumer, and lawful, and to defend its own right to some sort of "exclusivity" period for its generic diltiazem ER product, is an utter failure. Teva calls upon FDA to give full effect to the commercial marketing trigger in this case by ruling that the 180-day delay period applicable to generic diltiazem ER began when the deal between Andrx and HMR was concluded, or at the least when the first payment to Andrx under that deal was made. Only in this way can the agency uphold the intent of the law and protect the public from collusive statutory manipulation of the kind Andrx and HMR seek to achieve.

Respectfully submitted,



Geoffrey M. Levitt

Tuesday May 4, 8:10 am Eastern Time

Company Press Release

Faulding Resolves US Patent Litigation With Hoechst Marion Roussel, Inc.,

Faulding's Generic Version of Cardizem(R) CD to be Marketed Under License.

UNDERDALE, South Australia--(BUSINESS WIRE)--May 4, 1999-- International pharmaceutical and health care company F H Faulding & Co Limited (Faulding) today announced it has entered into a settlement of its patent litigation with Hoechst Marion Roussel, Inc. (HMRI) relating to Faulding's Abbreviated New Drug Application (ANDA) for diltiazem hydrochloride extended-release capsules, Faulding's proposed generic version of Cardizem® CD brand capsules. Cardizem® CD is indicated for the treatment of hypertension and chronic stable angina. According to IMS America, U.S. brand sales in 1998 were approximately US$630 million.

Under the agreement, all claims and counterclaims asserted by the parties will be dismissed, and Faulding has been granted a license under HMRI's patent to market its generic version of Cardizem® CD upon Faulding's receipt of final approval of its ANDA from the US Food and Drug Administration.

As part of the settlement, Faulding acknowledged that the HMRI patent on Cardizem® CD is valid and enforceable, and agreed to pay a royalty to HMRI on its sale of the product in the US market, once the Faulding product is launched. The settlement did not involve any immediate monetary payment by either party.

Faulding received tentative approval of its ANDA for this product in October 1998. The approval was characterized as tentative due to the pendency of the patent litigation between Faulding and HMRI and the entitlement of Andrx Corporation to a 180-day period of generic market exclusivity with respect to the product. With the resolution of its patent litigation, Faulding will be able to market its product after the 180-day exclusivity period has expired. The initiation of the exclusivity period will occur either with the commercial launch of the Andrx product or the entry of a final, non-appealable judgment of non-infringement or invalidity of the HMRI patents in Andrx's pending court case.

Andrx received final FDA approval of its ANDA in July 1998, but has not yet launched the product. At the present time, no other competitor has received final or tentative approval of an ANDA for a generic version of Cardizem® CD.

Faulding is a diversified world-wide health and personal care company, listed on the Australian Stock

Exchange. Faulding's principal businesses are generic oral and injectable pharmaceuticals, consumer health products, the provision of distribution and retail management services to pharmacies and logistics management services to hospitals. Faulding markets its products to and has representation in over 70 countries.

N.B. Faulding Company Announcements are posted to the Faulding website www.faulding.com

Note: Cardizem® CD is a registered trademark of Hoechst Marion

Roussel, Inc.

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